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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,845	10/18/2001	Samy Ashkar	CMCC 779	7069

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PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361

EXAMINER	
DEBERRY, REGINA M	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/981,845	ASHKAR ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *11 May 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-6*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): The objection to the specification, as set forth at page 3 of the previous Office Action (13 February 2004) is withdrawn in view of Applicant's amendment.

The rejection of claims 1-6 under 35 USC 112, First Paragraph, Written Description (New Matter), as set forth at pages 3-4 of the previous Office Action (13 February 2004) is withdrawn in view of Applicant's amendment.

The rejection of claim 1 under 35 USC 112, Second Paragraph, as set forth at page 8 of the previous Office Action (13 February 2004) is withdrawn in view of Applicant's amendment.

Continuation of 5. does NOT place the application in condition for allowance because: claims 1-6 remain rejected under 35 USC 112, First Paragraph, Scope of Enablement. The basis for this rejection is set forth at pages 4-8 of the previous Office Action (13 February 2004)

Applicant argues that one of ordinary skill in the art would be able to ascertain the functional binding activity of the peptides to integrins found on the surface of any cell type based upon the disclosure and the assays taught in the specification. Applicant argues that integrins are the principle receptors on animal cells for binding most extracellular matrix proteins, including collagen, fibronectin, and laminin, thus they are found on the surface of numerous cell types. Applicant maintains that although the specification uses osteoprogenitor cells as an example, one of ordinary skill in the art would know that osteopontin-derived peptides of the invention would be able to interact with integrins found on diverse cell types such as those recited in claim 6.

Applicant states that the Examainer suggests that the data demonstrating the binding of SEQ ID NO:15 to alpha5beta3 in Table 8 cannot be extrapolated to SEQ ID NO:11 (or any other osteopontin derived peptide) binding to any integrin on any cell type, because SEQ ID NO:15 was still able to cause human osteoprogenitor cells to attach and spread in the presence of antibodies against CD44 and alphabeta1. Applicant argues that just because the antibodies against CD44 and alphabeta1 failed to inhibit cell attachment and spreading does not mean that the peptide does not bind to these particualr receptors. Applicant contends that it likely means that the peptide induced cell migration and cell spread in osteoprogenitor cell may preferentially occur through a specific integrin or integrins i.e. alpha5beta3. Applicant states that other integrins may modulate this activity in other cell types. Applicant cites Turk et al. which describes the osteopontin induced migration of several epithelial lines. Different cell lines bind and spread through different integrins. Applicant cites Hu et al. Applicant argues that osteopontin binds to alpha5beta3 and antibodies to this integrin would not block osteopontin induced migration of a cell line that did not spread through this particular integrin. Applicant contends that osteopontin derived peptides besides SEQ ID NO:15 would bind to integrins due to sequence homology between the peptides and the presence of the required motifs recognized by integrins.

Applicant's arguments have been fully considered but are not deemed persuasive. Firstly, the references submitted are directed to full length osteopontin which is 314 amino acids long. The instant invention is drawn to OPN fragments which range from 33 to 63 amino acids. The specification fails to teach that the various OPN fragments all cell bind and spread through "any integrin receptor". Thus Applicant cannot assume that the claimed OPN fragments will bind those integrins as taught in the references. Furthermore, the art teaches that polypeptide changes such as deletions fragments or mutations can affect the activity of a protein. Thus, just because the OPN fragment may have an motif recognized by integrins does not mean it will act accordingly. The art also teaches proteins which share sequence homology, but have different activity. Secondly, the submitted references fail to teach that full length osteopontin can bind "any integrin". The references also teach that different cells express different integrins. Thus the type of integrin expression depends on the type of cell.

As was stated in the last Office Action, the specification teaches that SEQ ID NO:15 enables human osteoprogenitor cells to bind and spread through integrin alpha5beta3. The specification only teaches that SEQ ID NO:11 (elected species) enables human osteoprogenitor cells to bind and spread. The specification failed to teach that this action occurs through "any integrin".
It would be undue experimentation for one of skill in the art to first discern which cell type expressed a particular integrin then test for specific cell binding and spreading of the cell to OPN fragments by using antibodies against those specific integrins. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER